3. The non-technical abstract

Cosmo Bioscience is planning a first time in human, phase I/II clinical evaluation of Transgenic Lymphocyte Immunization (TLI) vaccination in subjects with histologically proven prostate adenocarcinoma.

The proposed clinical evaluation of TLI vaccination will consist of the intravenous administration of autologous lymphocytes transfected with non-viral (plasmid) DNA. The initial Phase 1 clinical study will involve as many as 20 subjects with prostate cancer. Subjects will be immunized following screening and selection as detailed in the proposed protocol. Each participant will complete approximately 9 visits over a three month period from the time the investigational treatment is administered.

The methods and procedures upon which the treatment is based were developed by Maurizio Zanetti M.D., Professor of Medicine/Member of the University of California San Diego (UCSD) Cancer Center, and his team at UCSD, and are covered by issued and pending patents which have been licensed to Cosmo Bioscience.

For the purpose of the study, the plasmid DNA will be manufactured under contract according to Good Laboratory Practices (GLP) by Althea Technologies Inc., a San Diego-based company specialized in manufacturing DNA for clinical trials. Althea will establish a Master Cell Bank and a Working Cell Line, and perform all of the required quality controls including proper characterization and purity of the plasmid DNA before it is released for clinical use. Althea has agreed to provide access to the required areas in the Biologics Master File on file with CBER. Althea will also provide documentation of the production processes utilized as well as the specific post production testing.

The product that will be injected into subjects, (i.e., autologous lymphocytes rendered transgenic with plasmid DNA), will be prepared under contract at Molecular Medicine Bioservices Inc., a San Diego-based company specialized in GMP services for gene therapy/cell therapy trials. Subject's peripheral blood will be drawn at the NIH-designated General Clinical Research Center (GCRC) and transported to Molecular Medicine immediately after collection. Molecular Medicine will process the subject's cells with the plasmid DNA that will be defined in the CMC section of the IND. Briefly, the subject's lymphocytes and plasmid DNA will be incubated in the absence of the serum proteins for 60 minutes at 37°. Neither exogenous carrier molecules nor facilitating electrical fields will be used for the transfection event, to ensure that there will be minimal if any effect on cell viability and function. For the purpose of this protocol, Cosmo Bioscience will instruct and supervise Molecular Medicine personnel so that the procedure will be executed with maximal reliability. Molecular Medicine has agreed to provide access to their Biologics Master File on file with CBER and will provide documentation of the production process as well as the specific post processing testing to insure identity, purity, potency and endotoxin level. Following transfection at Molecular Medicine the subject's lymphocytes will be transported to the NIH-designated UCSD GCRC for intravenous infusion.

The clinical trial will be conducted at the NIH-designated GCRC located at the UCSD Medical Center in San Diego. The entire clinical trial will be performed and monitored by a team lead by Maurizio Zanetti M.D., and composed of personnel from NIH-GCRC, the Clinical Trials Office of the NCI designated UCSD Cancer Center, and Cosmo Bioscience. The proposed protocol will involve a dose escalation study with the possibility of up to six escalating dosages to be evaluated. Subjects enrolled in the study will be given comprehensive evaluation. On the day of the injection of the transgenic autologous lymphocytes the subjects will be admitted to the GCRC and kept there for 24 hours under observation. The protocol will provide details as to the frequency and type of proposed evaluations to be conducted during this treatment and subsequent follow-up visits. Dose limiting toxicity criteria will be described in the protocol. It is anticipated that two subjects will be evaluated in each dosage level. We intend to follow subjects in each dose group for 30 days before proceeding to the next dose level. All subjects receiving treatment will be followed for three months. Standardized NCI toxicity evaluation criteria will be utilized to grade and categorize all adverse events (AE).